

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 11 April 1997 (11.04.97)	
International application No. PCT/IB96/00943	Applicant's or agent's file reference P16091WO/HGH
International filing date (day/month/year) 30 August 1996 (30.08.96)	Priority date (day/month/year) 01 September 1995 (01.09.95)
Applicant ABRIGNANI, Sergio	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

26 March 1997 (26.03.97)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Beate Giffo-Schmitt
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 730.91.11

PATENT COOPERATION TREATY

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From the INTERNATIONAL BUREAU

To:

HALLYBONE, Huw, George
Carpmaels & Ransford
43 Bloomsbury Square
London WC1A 2RA
ROYAUME-UNI

NOTIFICATION OF THE RECORDING
OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

Date of mailing (day/month/year) 11 February 1998 (11.02.98)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference P16091WO/HGH	
International application No. PCT/IB96/00943	International filing date (day/month/year) 30 August 1996 (30.08.96)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address

BIOCINE S.P.A.
Via Fiorentina, 1
I-53100 Siena
Italy

State of Nationality

IT

State of Residence

IT

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☒ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

CHIRON S.p.A.
Via Fiorentina, 1
I-53100 Siena
Italy

State of Nationality

IT

State of Residence

IT

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☐ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Carlos Roy

Telephone No.: (41-22) 338.83.38

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

To:

HALLYBONE, Huw George
CARPMAELS & RANSFORD
43 Bloomsbury Square
London WC1A 2RA
GRANDE BRETAGNE

Date of mailing
(day/month/year)

21. 11. 97

Applicant's or agent's file reference
P16091WO/HGH

IMPORTANT NOTIFICATION

International application No.
PCT/IB96/00943

International filing date (day/month/year)
30/08/1996

Priority date (day/month/year)
01/09/1995

Applicant
BIOCINE SPA et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



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Authorized officer

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P16091WO/HGH	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)
International application No. PCT/IB96/00943	International filing date (day/month/year) 30/08/1996	Priority date (day/month/year) 01/09/1995
International Patent Classification (IPC) or national classification and IPC C07K14/705		
Applicant BIOCINE SPA et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 26/03/1997	Date of completion of this report 21. 11. 97
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Kronester-Frei, A Telephone No. (+49-89) 2399-8555 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB96/00943

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-35 as originally filed

Claims, No.:

1-20 as originally filed

Drawings, sheets:

1/14-14/14 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IB96/00943

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 11.

because:

- ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

cf Separate Sheet, item 7
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IB96/00943

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims..
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 4-10 (in part)
	No: Claims 4-10 (in part)
Inventive step (IS)	Yes: Claims
	No: Claims 4-10(in part)
Industrial applicability (IA)	Yes: Claims 4-10
	No: Claims

2. Citations and explanations

cf Separate Sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IB96/00943

VI. Certain documents cited

1. Certain published documents (Rule 70.10)
2. Non-written disclosures (Rule 70.9)

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

cf Separate Sheet, item 4

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IB96/00943

1. The following documents are mentioned for the first time in this Preliminary Report; the numbering is identical to the order used in the International Search Report and will be adhered to in the rest of the procedure:

D1 to D4

2. The priority documents pertaining to the present application were not available at the time of establishing this first written opinion. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the documents 2 and D4 cited in the International Search Report could become relevant to assess whether the claims under examination satisfy the criteria set forth in Article 33(1) PCT.
3. As far as claims 4 to 10 read without fragments of the 24kD protein, novelty of the process claimed can be acknowledged, since in D1 and D3 no such combination of procedural features combined with the antigen of 24kD molecular weight has been disclosed.
As far as fragments of the 24kD protein are concerned novelty is lacking since in D1 several shorter antigens having the same functional property have been disclosed which fall within the disclosure of these claims.
4. However it would appear that in principle product claims could be amended to satisfy the requirements of Articles 33(2)(3)PCT and 5/6 PCT, if such claims would be drafted in a product-by-process form and if the known protein fragments of D1 which interact and bind an HCV antigen E2/NS1 would not be embraced.
In order to highlight the situation the examiner is prepared to explain the particular situation of products claims although these

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IB96/00943

claims shall not be examined for the reasons given under item III 5.

The protein mentioned in claims 1 to 3 and their dependent subject-matter has not been disclosed in a manner sufficiently clear to enable a person skilled in this art to understand the subject-matter and to become able to rework the application (Art. 5 and 6 PCT).

In fact the unique technical information given in claim 1 is that a 24kD protein and fragments thereof are concerned which have one specific binding property or a functional equivalent thereof. It is understood from the description (page 2, lines 27-30, page 3, lines 11/12, 22, 32/33, page 4, line 5 to page 5, line 29) that a series of technical requirements and procedural steps should be present to arrive at the protein claimed and that in addition minimum requirements should be present:

The protein is unglycosylated, the protein is provided by cell membranes. The description shows that the process starts from particular cells, i.e. MOLT-4 cells or at least from cells which show a HCV infection susceptibility. The protein seems to be a transmembrane protein, the ability to bind to the E-protein is expressed as a minimum requirement,.

The process involved necessarily has to start from culturing these particular cells and to purify them in a particular manner according to the process disclosed in claim 10. The dependent subject-matter claimed in claims 12 to 18 seems to satisfy the requirements of patentability if they depend on patentable product-by-process claims.

In the absence of any of those additional technical and procedural features in product claims, the burden to carry out extensive experimental studies to rework the application would be shifted in an undue manner to the public.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/IB96/00943

5. Since the specification does not disclose any DNA related information claims 19 and 20 relate to speculative subject-matter which does not satisfy the requirements of Article 5 PCT.
6. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D3 are not mentioned in the description, nor are these documents identified.
7. For the assessment of the present claims 11 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07K 14/705, G01N 33/00	A1	(11) International Publication Number: WO 97/09349 (43) International Publication Date: 13 March 1997 (13.03.97)
(21) International Application Number: PCT/IB96/00943 (22) International Filing Date: 30 August 1996 (30.08.96) (30) Priority Data: 9517926.3 1 September 1995 (01.09.95) GB (71) Applicant (for all designated States except US): BIOCINE S.P.A. [IT/IT]; Via Fiorentina, 1, I-53100 Siena (IT). (72) Inventor; and (75) Inventor/Applicant (for US only): ABRIGNANI, Sergio [IT/IT]; Piazza Roma, 13, I-53035 Monteriggioni (IT). (74) Agent: HALLYBONE, Huw, George; Carpmaels & Ransford, 43 Bloomsbury Square, London WC1A 2RA (GB).		(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: BINDING PROTEIN (57) Abstract A functionally unglycosylated transmembrane protein having a molecular weight of about 24kd which is ubiquitous in human cells and exhibits the same species specificity as hepatitis C virus. The protein is capable of binding to HCV surface proteins and is a putative HCV cellular receptor. As such it has many applications in the fields of diagnosis and treatment of HCV infection and in the design of HCV therapeutics.		

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P16091WO/HGH	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/IB 96/00943	International filing date(day/month/year) 30/08/1996	(Earliest) Priority Date (day/month/year) 01/09/1995
Applicant BIOCINE SPA et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).
2. ☐ Unity of invention is lacking (see Box II).
3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
 - ☐ filed with the international application.
 - ☐ furnished by the applicant separately from the international application,
 - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
 - ☐ Transcribed by this Authority
4. With regard to the title, ☒ the text is approved as submitted by the applicant.
 - ☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,
 - ☒ the text is approved as submitted by the applicant.
 - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:
 - Figure No. ☐ as suggested by the applicant.
 - ☐ because the applicant failed to suggest a figure.
 - ☐ because this figure better characterizes the invention.
 - ☒ None of the figures.

INTERNATIONAL SEARCH REPORT

National Application No.

/IB 96/00943

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07K14/705 G01N33/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO,A,93 04205 (ABBOTT LABORATORIES) 4 March 1993 see the whole document ---	16-18
X,P	WO,A,96 05513 (BIOCINE S.P.A.) 22 February 1996 see the whole document ---	
A,P	WO,A,96 04376 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA) 15 February 1996 see the whole document --- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

23 December 1996

Date of mailing of the international search report

17. 01. 97

Name and mailing address of the ISA

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Authorized officer

Panzica, G

INTERNATIONAL SEARCH REPORT

International Application No.

IB 96/00943

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,P	<p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 93, no. 5, March 1996, WASHINGTON US, pages 1756-1763, XP000615446</p> <p>ROSA D. ET AL.: "A quantitative test to estimate neutralizing antibodies to the hepatitis C virus: Cytofluorimetric assessment of envelope glycoprotein 2 binding to target cells"</p> <p>see the whole document</p> <p>-----</p>	

INTERNATIONAL SEARCH REPORT

on patent family members

onal Application No

/IB 96/00943

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9304205	04-03-93	US-A- 5308750 AU-A- 2585092 CA-A- 2115923 EP-A- 0603307 JP-T- 6510192	03-05-94 16-03-93 04-03-93 29-06-94 17-11-94
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WO-A-9605513	22-02-96	AU-A- 3189495 CA-A- 2174212 EP-A- 0723665	07-03-96 22-02-96 31-07-96
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WO-A-9604376	15-02-96	AU-A- 3238995	04-03-96
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